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Pericardial Abnormalities in Gaucher's Disease

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Gaucher's disease may present with various clinical features. Pericardial disorders have not received the attention they deserve in association with this condition, and the following is a report of three cases showing these features.

CASE 1

A woman, now aged 22 years, had been well throughout infancy and childhood, apart from a tendency to excessive bleeding after trauma and occasional prolonged epistaxes. She was first admitted to hospital at the age of 14 years for investigation of heavy bleeding after dental extractions.

Family History. An elder sister and her father's cousin both had Gaucher's disease. All were Ashkenazi Jews.

Clinical Findings on First Admission (aged 14 years). There were numerous ecchymoses over the legs, with hepatosplenomegaly.

Investigations revealed Hb 87 g./100 ml.; WBC 5700/cu.mm. (normal differential count); platelets 56,000/cu.mm.; ESR (Westergren) 10 mm./1 hr.; sternal marrow cellular, with 0·8 per cent typical Gaucher cells; electrocardiogram normal; chest *x*-ray normal; *x*-ray femora, lower halves expanded with loss of the normal concavity above the epiphyses. Cortices thin at lower ends with generalized loss of bone density. Irregular trabeculation in the upper shaft with cystic resorption in the subtrochanteric region. Other systems normal on *x*-ray examination.

The diagnosis of Gaucher's disease was confirmed and the patient discharged. At the age of 17, ^{57}Cr red cell survival was normal.

Second Admission (age 21 years). The patient was admitted with a four-hour history of severe central retrosternal pain radiating into the neck, and aggravated by coughing and deep breathing. A similar episode of pain had occurred one year before, but this had subsided spontaneously.

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Clinical Findings. Temperature 37°C. She was anaemic, with sallow complexion. There were bilateral pingueculae, and multiple ecchymoses over the legs. The liver was enlarged 2 cm. and the spleen was 3 cm. below the costal margin.

The pulse rate was 104 a minute with paradox. BP 110/60 mm. Hg; jugular venous pressure +8 cm., with positive Kussmaul's sign. The area of cardiac dullness was normal, but the apex was impalpable and heart sounds were distant, with a pleuropericardial rub.

Investigations revealed Hb 11·2 g./100 ml.; mean corpuscular haemoglobin concentration, 31 per cent; film showed hypochromia and anisocytosis; WBC, 5000/cu.mm. (59% N, 40% L, 1% M); ESR (Westergren), 26 mm./1 hr.; platelets, 94,000/cu.mm.; prothrombin time, 16 sec. (control 13 sec.); clotting time, 7 min.; bleeding time, 8 min. (normal 2–5 min.); antistreptolysin 0 titre 50 units/ml.; SGOT, 22 IU; bilirubin, 0·5 mg./100 ml.; total serum proteins, 7·1 per cent; electrophoresis, normal; serum alkaline phosphatase, 4·4 K-A units; formol stable acid phosphatase, 11·7 units (normal 0·5–5·0); blood urea, 32 mg./100 ml.; serum iron, 75 mg./100 ml.

Chest *x*-ray showed generalized cardiac enlargement, with the configuration of a pericardial effusion; electrocardiogram showed sinus tachycardia 125/min., with normal voltage; ST segment elevation in all leads except III and aVR; serial records over three weeks showed a gradual return to normal.

Progress. During her stay in hospital she had a further episode of pericarditis and in the subsequent few months two further transient attacks. These were all associated with pain and a pericardial rub.

In view of the bleeding tendency, it seemed likely that the recurrent pericarditis was due to haemorrhage into the pericardium. As there was a possibility of provoking further bleeding, diagnostic aspiration was not performed.

CASE 2

This patient, now aged 30 years, is the elder sister of Case 1. The notes were destroyed in a microfilming process, but she is known to have Gaucher's disease with hepatosplenomegaly and Gaucher's cells in the

marrow. At the age of 21, over a period of about 6 months, she had 4 episodes of pericarditis with pain, a pericardial rub, and electrocardiographic changes of pericarditis. Platelet counts during these episodes varied from 60,000 to 80,000/cu.mm. The cause of the recurrent pericarditis was unknown, and no further episodes have occurred since that time.

Case 3

A man aged 53 years, with no known Jewish ancestry, was well until the age of 26 when, after a short history of dyspnoea and abdominal distension, he was admitted to hospital. Findings included a haemopericardium, which was twice aspirated, and hepatosplenomegaly. Splenectomy was later performed and the diagnosis of Gaucher's disease confirmed. An elder sister had had a splenectomy for Gaucher's disease in the same hospital four years earlier, at the age of 25.

The patient was subsequently followed up until 1951 (age 36 years) during which time he remained well, with a normal Hb, white cell, and platelet count. Hepatomegaly persisted unchanged.

In 1962, at the age of 47, he complained of increasing dyspnoea and ankle oedema. He was treated for cardiac failure and atrial fibrillation with a good response. In 1968 his symptoms recurred and he was referred to hospital. On examination he was pigmented in the face, neck, and forearms, and had bilateral pingueculae. In the cardiovascular system there was atrial fibrillation, with signs of constrictive pericarditis and mitral regurgitation. The abdomen was distended with ascites and a firm liver enlarged to the level of the umbilicus.

There were no other abnormal physical signs.

Investigations revealed Hb, 90 per cent, normal indices; WBC, 11,300/cu.mm. (74% N, 7% E, 10% L, 9% M); platelets, 174,000/cu.mm.; ESR, 24 mm./hr.; bleeding, clotting, and prothrombin times normal; urea and electrolytes normal; alkaline phosphatase, SGOT, SGPT, and LDH normal; acid phosphatase 3·1 units/100 ml., of which 1·8 units were formol stable; BSP retention was 7·5 per cent at 45 minutes; Mantoux positive at 1:1000 dilution; electrocardiogram, atrial fibrillation, digoxin effect, and flat T waves; chest *x*-ray (Fig. 1) showed cardiac enlargement, with heavy calcification of the pericardium; sternal marrow: there was infiltration with cells of the Gaucher type (Fig. 2).

Cardiac catheterization confirmed the presence of constrictive pericarditis and moderate mitral regurgitation.

The patient was treated medically and subsequently submitted to pericardectomy (Mr. O. S. Tubbs). At operation the pericardium, which was found to be heavily calcified over both ventricles to 0·5 cm. thickness, stripped easily, except in 3 or 4 areas where there was calcific myocardial infiltration. Lung, liver, and mediastinal lymph node biopsies were taken.

Histology. The pericardium showed fibrous thickening and calcification, but there were no specific changes. The biopsies of the lung and the mediastinal nodes were both normal. In the liver, Gaucher cells were present in occasional sinusoids and also in sheets (Fig. 3), associated with some fibrous tissue and lymphocytes, which were not obviously confined to the portal tracts alone.

The patient's post-operative course was uneventful, the congestive failure abating, but atrial fibrillation persisted.

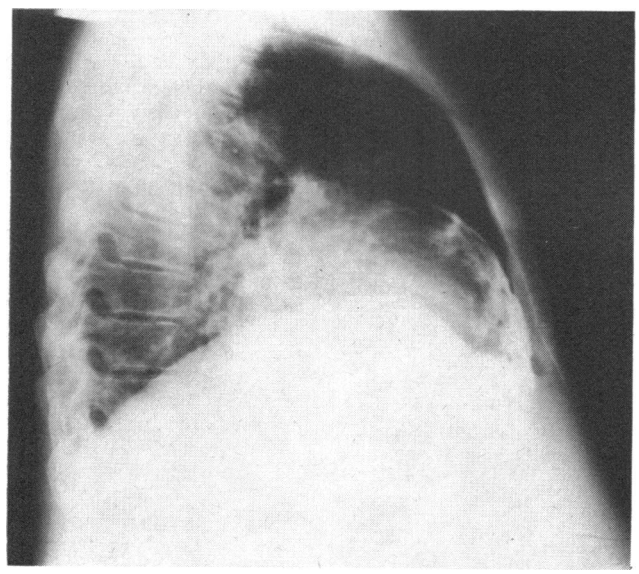

Fig. 1.—Chest *x*-ray (Case 3) shows extensive pericardial calcification.

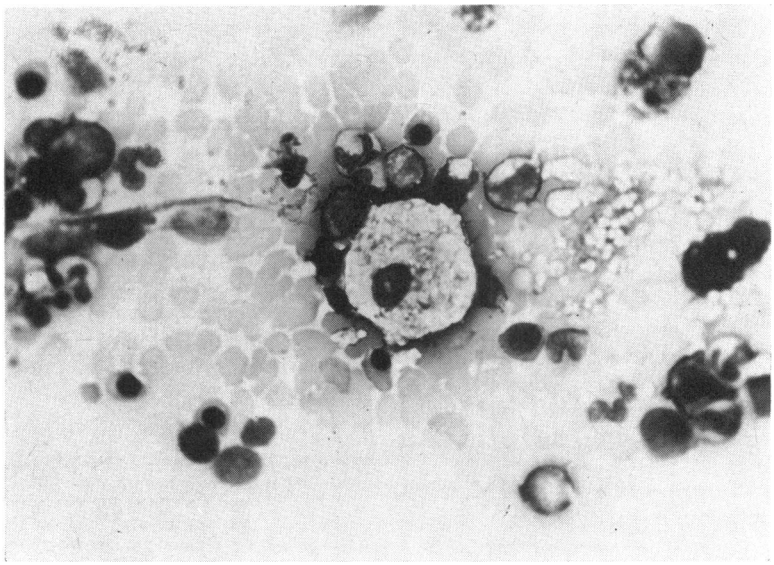

FIG. 2.—Typical Gaucher cell in bone-marrow smear from Case 3. (×450.)

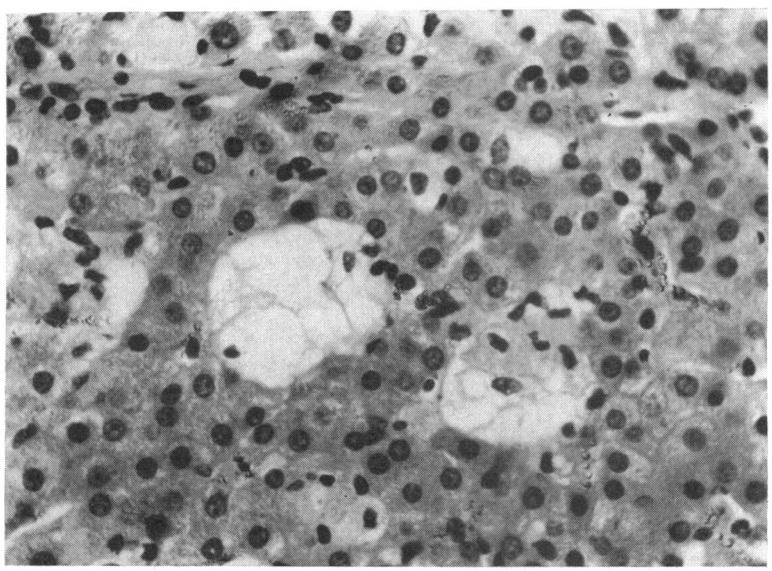

FIG. 3.—Gaucher cells in the liver of Case 3. (×395.)

DISCUSSION

A review of the published reports has revealed only three cases of Gaucher's disease associated with pericardial abnormalities. Zlotnick and Groen (1961) described a 47-year-old woman with Gaucher's disease and a haemorrhagic diathesis. Terminally she was found to have cardiomegaly and massive pericardial calcification. Subsequent histology showed no definite cause for the calcification, though the authors suggested it might have been due to organization of an unrecognized pericardial haemorrhage.

Roberts and Fredrickson (1967) reported a 30-year-old man who, after two years of recurrent chest pain, cardiac arrhythmias, and increasing pulmonary hypertension, developed a massive haemopericardium and tamponade. Necropsy revealed "raging diffuse haemorrhagic pericarditis" but no

Gaucher cells were identified. The pulmonary hypertension was thought to be due to extensive infiltration of the alveolar capillaries with Gaucher cells.

The third case (Benbassat *et al.*, 1968) was a 29-year-old man who developed constrictive pericarditis requiring pericardectomy. The fibrotic tissue removed consisted of acellular collagen fibres, occasional lymphocytes, and scattered macrophages containing haemosiderin pigment. No Gaucher cells were seen. Necropsy two months later did not provide any additional information. The authors suggest a direct association between Gaucher's disease and constrictive pericarditis due to unrecognized pericardial haemorrhage and subsequent organization. They offer the evidence of extensive haemosiderosis in the pericardium as explanation of this.

In Cases 1 and 2 there was a haemorrhagic diathesis and strong presumptive evidence that pericarditis was due to recurrent haemorrhage. The reason why such an unusual complication should occur at about the same age in sisters remains unexplained. In Case 3, proven haemopericardium had been followed 25 years later by constriction and calcification. The suggestion that constrictive pericarditis might follow intrapericardial haemorrhage was first made by Dániel and Puder in 1932 and by several others (White, 1937; Ada, Jones, and Sheeran, 1950; Naclerio, Maynard, and Cordice, 1953) since then. In a review of the reports, Ehrenhaft and Taber (1952) described experimental studies with 14 dogs. In one group, injected intrapericardially with autogenous blood, pericardial scarring occurred without constriction. In a second group, injected with the lipid fraction of blood, there was more conspicuous pericardial thickening with adhesions, and one of six dogs died of constrictive pericarditis with early calcification.

From a clinical standpoint trauma is a common cause of haemopericardium and subsequent constrictive pericarditis is well documented (Glenn, 1940; Kerley, 1948; McKusick, Kay, and Isaacs, 1955; Barker and Johnston, 1950; Overholt *et al.*, 1952; Ehrenhaft and Taber, 1952; Deterling and Humphreys, 1955). Despite this, Wood (1961) did not observe this complication in 30 cases of penetrating cardiac injury, nor had he ever encountered it after mitral valvotomy, despite post-operative haemorrhagic pericarditis developing in 10 per cent of his cases.

A haemorrhagic diathesis is a common feature of Gaucher's disease, yet intrapericardial haemorrhage has only been described in 6 out of over 300 cases reported. Though a rare complication, we agree with previous authors in believing that, as a result of this haemorrhagic tendency, patients with Gaucher's disease may develop pericardial constriction and calcification.

Summary

Three cases of Gaucher's disease are described where intrapericardial haemorrhage is thought to have been responsible for recurrent pericarditis in two and constrictive pericarditis in the third. In addition, three previously reported cases have been reviewed and evidence has been presented to suggest that the association between pericardial disease and Gaucher's disease may be direct and due to the haemorrhagic diathesis common to the latter condition.

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